REMARKS

Upon entry of the amendment, claims 8, 9, 11 to 17 and 24 will be pending.

Claim 10 is cancelled herein without disclaimer, and without prejudice to Applicant's pursuing prosecution of subject matter encompassed within the claim in an application claiming the benefit of priority of the subject application.

New claim 24 has been added. The new claim is supported by claims 8 and 10 as originally filed and, therefore, does not add new matter. Furthermore, the new claim does not require a new search or consideration because the subject matter of the new claim has been of issue in this case. It is submitted that the amendments place the claims in condition for allowance, or in better condition for appeal. In addition, a finally rejected claimed was cancelled such that the amendment does not result in a greater number of claims pending than were pending prior to the final Office Action. As such, entry of the amendments is respectfully requested.

A. Rejection Under 35 U.S.C. 112, First Paragraph (Enablement)

The rejection of claim 10 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, is respectfully traversed. Although claim 10 has been cancelled, the rejection is relevant to new claim 24 and, therefore, is addressed with respect to the new claim.

Applicant respectfully disagrees that the specification allegedly does not teach one skilled in the art how to ameliorate an immune response mediated disorder selected from AIDS, autoimmune disease, and graft rejection. The Examiner states that there is no passive antibody based therapy that can ameliorate HIV, providing the Fahey et al. reference in support of this position. Applicant submits, however, that the standard for enablement is not whether a method corresponding to the claimed invention has been demonstrated. Instead, the test for enablement

is whether undue experimentation would have been required for one skilled in the art to practice the claimed invention (*In re Wands*, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988); "the key word is 'undue', not 'experimentation'." *Id.* at page 1404).

The claims of the subject application are directed to a method of passive immunization to ameliorate an immune response mediated disorder such as AIDS. With respect to the factors for accessing enablement, as set forth in *Wands*, Applicant points out that the level of skill in the clinical arts is very high, and methods of passive immunization, as well as methods of performing clinical trials relating to such methods, are well known and routine. Furthermore, Applicant sets forth examples demonstrating that administration of an antibody capable of suppressing intercellular leukocyte adhesion, wherein the antibody binds to an epitope on the leukocyte adhesion receptor β-chain, can effectively inhibit syncitium formation and inhibit HIV gp120 binding by H52 (see specification, page 20, line 3 to page 25, line 23). It is submitted that, in view of such a disclosure, the skilled artisan would reasonably believe that the aforementioned inhibitory action can be predictive of results *in vivo*. Further in this respect, it is noted that the specification discloses methods for producing and characterizing antibodies contemplated for use in the present invention (see specification, page 5, line 22, to page 7, line 12), as well as guidance as to administration protocols and dosages for practicing the claimed methods (see, e.g., page 15, lines 1-14; and page 17, line 15 to page 18, line 25). Based on this disclosure, it is submitted that the skilled artisan would have known that only clinical trials as are routinely performed in the art would be required to ameliorate an immune response mediated disorder such as AIDS according to the claimed methods.

In support of Applicant's position that the skilled artisan reasonably would have known that a passive immunization method can be useful for ameliorating an immune response mediated disorder such as AIDS, the Examiner's attention is directed to Exhibit A, which is a page of the U.S. government clinical trials web site (on the world wide web, at the URL "clinicaltrials.gov") that was identified by a search using the terms "passive immunization" and "HIV". As is clear from Exhibit A, a number of clinical trials directed to passive immunization

for treating AIDS are in progress. Such trials include, for example, a phase I trial using anti-HIV gp120 monoclonal antibodies (see Exhibit B), which, it is submitted, is analogous to the claimed methods of administering an antibody, as well as a phase III trial using anti-HIV immune serum globulin (Exhibit C). Thus, despite the alleged teaching of Fahey et al. that "the results obtained in trials using **numerous different types** of immune-based therapies have not achieved success (See table 1)" (OA at page 3, emphasis in original), in fact, those skilled in the art believe that passive immunotherapy can be useful for treating AIDS as evidenced by Exhibits A to C submitted herewith. It is noted that Exhibits A to C are provided only in support of Applicant's position that the subject application was enabling at the time of filing (see, for example, *Gould v. Quigg*, 3 U.S.P.Q.2d 1302 (Fed. Cir. 1987)).

For the above reasons, Applicant maintains that the specification provides ample guidance such that the skilled artisan would have known how to practice the invention commensurate in scope with previously pending claim 10 (and new claim 24) without undue experimentation. Accordingly, reconsideration and withdrawal of this rejection under 35 U.S.C. § 112, first paragraph, are respectfully requested.

B. Rejections Under 35 U.S.C. § 102

The rejection of claims 8, 9, 11, and 13-15 under 35 U.S.C. § 102(e) as allegedly being anticipated by Arfors (U.S. Patent No. 4,797,277), is respectfully traversed.

It is submitted that Applicant's invention, as defined by claim 8, distinguishes over Arfors by requiring a method of ameliorating an immune response **mediated** disorder in an animal by administering to the animal a therapeutically effective amount of an antibody, capable of suppressing intercellular leukocyte adhesion, wherein the antibody binds to an epitope on the leukocyte adhesion receptor β-chain (LAR-β). Arfors does not teach or suggest such a method. Instead, Arfors describes methods for treating ischemia/reperfusion-induced tissue damage. Indeed, Arfors is silent with respect to ameliorating an immune response **mediated** disorder.

The Examiner states that Arfors discloses administering an antibody that binds an epitope of LAR-β to prevent ischemia/reperfusion-induced tissue damage, and further states that "Ischemia leads to necrosis, thus Arfors is ameliorating an immune response mediated disorder in that **necrosis involves an immune response** (inflammation) at the site of injury." (OA at page 6; emphasis added). While Applicant does not dispute that an immune response may be involved in necrosis that may occur due to ischemia/reperfusion injury, ischemia/reperfusion injury is an activated oxygen species mediated disorder, not an immune response mediated disorder. The role of activated oxygen species in reperfusion injury is described by Rubin and Farber (Pathology 3d ed. 1998; pages 17-22, which are attached hereto as Exhibit D). Rubin and Farber mention that an inflammatory response occurs in reperfusion due to the release of hydrolytic enzymes and activated oxygen species by neutrophils, but do not mention any role for an immune response in reperfusion injury.

Applicant maintains that one of ordinary skill in the art would not consider ischemia/reperfusion-induced tissue damage to be an immune response mediated disorder, as required by the claims. In this respect, it is submitted that one of ordinary skill in the art, viewing the Arfors reference, would not reasonably have known that the methods of Arfors could be used to ameliorate an immune response mediated disorder. As such, Arfors cannot anticipate the claimed methods. Accordingly, reconsideration and withdrawal of the rejection of claims 8, 9, 11, and 13-15 under 35 U.S.C. § 102(e) are respectfully requested.

The rejection of claim 8 under 35 U.S.C. § 102(b) as allegedly being anticipated by Vedder, et. al., is respectfully traversed. Like Arfors, Vedder et al. describes methods for treating ischemia/reperfusion-induced tissue damage. Indeed, like Arfors, Vedder et al. is silent with respect to ameliorating an immune response mediated disorder.

Vedder et al. describe a role of neutrophils in causing organ injury due to ischemia/reperfusion due to the release of proteases, toxic oxygen metabolites, and vasoactive substances. However, for the reasons set forth with respect to Arfors, it is submitted that Vedder

et al. do not describe an immune response mediated disorder, or a method of ameliorating an immune response mediated disorder and, therefore, does not anticipate the claimed invention. Accordingly, reconsideration and withdrawal of the rejection of claim 8 under 35 U.S.C. § 102(b) are respectfully requested.

C. Rejections Under 35 U.S.C. § 103(a)

The rejection of claims 8, 9, 11, and 13-15 under 35 U.S.C. 103(a) as allegedly being unpatentable over Arfors and Vedder, et al. in view of Springer, et. al., is respectfully traversed. Arfors and Vedder, et al. are applied as described above. Springer, et al. describe methods relating to the use of proteins (but not antibodies) for treating an immune response mediated disorder such as allograft rejections. Springer et al. generally describe antibodies specific for LAC components and the use of such antibodies for diagnostic purposes, but do not teach or suggest the use of such antibodies to ameliorate an immune response mediated disorder. Instead, Springer et al. describe the use of the polypeptide components of LAC (e.g., LFA-1), including peptides thereof, to treat an immune disorder (see page 12).

The Examiner states that motivation to combine the references is that the conditions described in the references lead to necrosis, which, in turn, can result in an immune response that leads to further necrosis and, therefore, that such necrosis is an immune response mediated disorder. As discussed above, and for the reasons of record, Applicant maintains that the skilled artisan would not consider necrosis to be an immune response mediated disorder and, therefore, that absent hindsight analysis in view of the present specification, one of ordinary skill in the art would not have been motivated to combine the references. Accordingly, reconsideration and withdrawal of the rejection of claims 8, 9, 11, and 13-15 under § 35 U.S.C. 103(a) are respectfully requested.

The rejection of claims 11 and 12 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Arfors, Vedder, et. al., and Springer, et. al., in view of Hildreth, et. al., is respectfully traversed. For the reasons set forth above and of record in this case, Applicant

maintains that one of ordinary skill in the art would not have been motivated to combine Arfors and/or Vedder et al. with Springer, et al. because one in the art would not consider necrosis to be an immune response mediated disorder. Further, there is nothing in the Hildreth et al. reference to provide that which is missing in Arfors, Vedder, et al. and/or Springer, et al.. As such, it is maintained that, absent hindsight analysis, there would have been no motivation to combine the cited references. Accordingly, reconsideration and withdrawal of the rejection of claims 11 and 12 under 35 U.S.C. § 103(a) are respectfully requested.

The rejection of claims 16 and 17 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Arfors, Vedder, et. al., and Springer, et. al., in view of Pastan, et. al., is respectfully traversed. As set forth above, one of ordinary skill in the art would not have been motivated to combine Arfors and/or Vedder et al. with Springer et al., and there is nothing in the Pastan reference to cure this deficiency. As such, motivation to combine the references is absent. Accordingly, reconsideration and withdrawal of the rejection of claims 11 and 12 under 35 U.S.C. § 103(a) are respectfully requested.

D. Double Patenting Rejection

Claims 8 to 17 are rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1 to 7 of U.S. Patent No. 5,888,508. Applicant acknowledges the rejection and will file a Terminal Disclaimer, disclaiming any term of a patent issuing from the subject application that may extend beyond the term of U.S. Patent No. 5,888,508, upon receiving an indication that the present claims otherwise are in condition for allowance.

In view of the amendments and above remarks, it is submitted that the claims are in condition for allowance, and a notice to that effect respectfully is requested. The Examiner is invited to contact Applicant's undersigned representative if there are any questions relating to this application.

Please charge any additional fees, or make any credits, to Deposit Account No. 50-1355.

Respectfully submitted,

Date: February 20, 2003

Lisa A. Haile, J.D., Ph.D.
Reg. No. 38,347
Attorney for Applicant
Telephone No.: (858) 677-1456
Facsimile No.: (858) 677-1465

USPTO CUSTOMER NUMBER 28213
GRAY CARY WARE & FREIDENRICH LLP
4365 Executive Drive, Suite 1100
San Diego, California 92121-2133